

FDA approves emicizumab-kxwh for prevention and reduction of bleeding in patients with hemophilia A with factor VIII inhibitors

On November 16, 2017, the Food and Drug Administration approved emicizumab-kxwh (HEMLIBRA, Genentech, Inc.) for routine prophylaxis to prevent or reduce the frequency of bleeding episodes in adult and pediatric patients with hemophilia A (congenital factor VIII deficiency) with factor VIII inhibitors.

Approval was based on data from two clinical trials—an adult and adolescent trial (HAVEN 1) and a pediatric trial (HAVEN 2). HAVEN 1 (NCT02622321) was a randomized, multicenter, open-label, phase 3 trial in 109 adult and adolescent males (aged 12 to 75 years and >40 kg) with hemophilia A with FVIII inhibitors who previously received either episodic (on-demand) or prophylactic treatment with bypassing agents. Patients on prior episodic treatment were randomized 2:1 to weekly emicizumab-kxwh prophylaxis (3 mg/kg once weekly for the first 4 weeks followed by 1.5 mg/kg once weekly, thereafter) or no prophylaxis. Patients randomized to no prophylaxis could switch to emicizumab-kxwh prophylaxis after 24 weeks. For patients receiving emicizumab-kxwh prophylaxis, the annualized bleeding rate (ABR) requiring treatment with coagulation factors was 2.9 (95% CI: 1.7, 5.0) compared with 23.3 (95% CI: 12.3, 43.9) for patients not receiving prophylaxis corresponding to an 87% ABR reduction (95% CI: 72.3%, 94.3%), $p=0.0001$. In addition, improvements in patient-reported hemophilia-related symptoms and physical functioning in patients receiving emicizumab-kxwh prophylaxis were

Feedback

HAVEN 2 (NCT02795767) was a single-arm, multicenter, open-label, clinical trial in pediatric males (age 12 years or 12-17 years who weigh ≥ 40 kg) with hemophilia A with FVIII inhibitors. Patients received emicizumab-kxwh prophylaxis at the dose and schedule described above. In 23 patients evaluated at the interim analysis, the ABR for treated bleeds was 0.2 (95% CI: 0.1, 0.6). The ABR for all bleeds was 2.9 (95% CI: 1.8,)

The most common adverse reactions (occurring in $\geq 10\%$ of patients taking emicizumab-kxwh) are injection site reactions, headache, and arthralgia. Cases of thrombotic microangiopathy and thrombotic events were reported when on average a cumulative amount of >100 U/kg/24 hours of activated prothrombin complex concentrate (aPCC) was administered for 24 hours or more to patients receiving emicizumab-kxwh prophylaxis. The prescribing information contains a boxed warning to monitor for thrombotic microangiopathy and thrombotic events when aPCC is administered. If symptoms occur, aPCC should be discontinued and emicizumab-kxwh should be suspended.

The recommended dose of emicizumab-kxwh is 3 mg/kg by subcutaneous injection once weekly for the first 4 weeks, followed by 1.5 mg/kg once weekly.

Full prescribing information is available at:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/761083s000lbl.pdf
(https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/761083s000lbl.pdf).

Emicizumab-kxwh was approved 3.3 months prior to the assigned regulatory action date. FDA granted Priority Review, Breakthrough Therapy designation, and Orphan Drug designation for this indication. A description of FDA expedited programs is in the Guidance for Industry: Expedited Programs for Serious Conditions-Drugs and Biologics, available at:

<http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm358301.pdf>
([/media/86377/download](http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm358301.pdf)).

Healthcare professionals should report all serious adverse events suspected to be associated with the use of any medicine and device to FDA's MedWatch Reporting System by completing a form online at <http://www.fda.gov/medwatch/report.htm> (<http://www.fda.gov/medwatch/report.htm>), by faxing (1-800-FDA-0178) or mailing the postage-paid address form provided online, or by telephone (1-800-FDA-1088).

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